The Unorthodox Loss of Propyl from the Molecular Ions of Methoxycyclohexane

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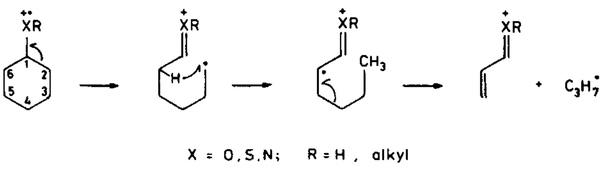
It is shown by field ionization kinetics, D and ^{13}C labelling and metastable ion studies that the loss of a propyl radical from the molecular ion of methoxycyclohexane occurs via two routes. At a molecular ion lifetime of $<10^{-10}$ s propyl is eliminated in the 'classic' way, i.e. by successive cleavage of the C(1)—C(2) bond, 1,5-H shift from C(6) to C(2) and cleavage of the C(4)—C(5) bond. At 10^{-10} s the other pathway for propyl loss starts to take place, which is initiated by a hydrogen shift from position 3 or 5 to the methoxy group. This leads in a series of steps to the formation of the 3-methoxyhexene-1 ion, which eventually eliminates a propyl radical. In some of the steps specific hydrogen–deuterium exchange processes have been observed.

INTRODUCTION

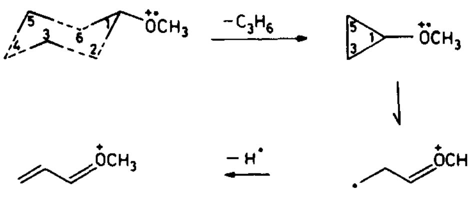
One of the archetypal reactions in mass spectrometry is the elimination of a propyl radical from monosubstituted cyclohexane molecular ions which in many cases leads to the most intense peak in the corresponding mass spectra. The mechanism of the reaction concerns the successive homolytic cleavage of the C(1)—C(2) bond, 1,5-H shift from C(6) to C(2) and homolytic cleavage of the C(4)—C(5) bond[1] as summarized in Scheme 1. This is also true for methoxycyclohexane (X = 0, R = CH_3). However, in 1970 Klein and Smith[2] postulated an additional mechanism (Scheme 2) for the formation of the $[M-C_3H_7]^+$ ion from this compound on the basis of extensive D labelling, which has shown that all four hydrogen atoms from the 2- and 6-position can be retained in the eliminated neutral species.



Scheme 1

Nowadays more advanced methods, such as field ionization kinetics (FIK)[3] and angle-resolved mass spectrometry (ARMS)[4] are available to study the mechanisms of ionic reactions in a mass spectrometer.

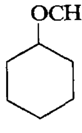
In the present study the FIK method in combination with D and ^{13}C labelling has been applied to obtain a time-resolved picture of the propyl loss from ionized methoxycyclohexane. This has indeed revealed a pathway in addition to the 'classic' route of propyl loss (Scheme 1), although essentially different from the one proposed earlier[2] (Scheme 2) as will be shown below.



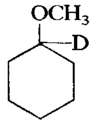
Scheme 2

RESULTS AND DISCUSSION

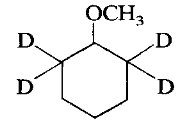
The base peak at m/z 71 in the 70 eV mass spectrum of methoxycyclohexane **1**, shown in Fig. 1, corresponds to the loss of propyl from the molecular ion. The shift of this peak in the spectra of the D-labelled analogues **1a–1e** is given in Table 1 and confirms the previous results of Klein and Smith.[2]



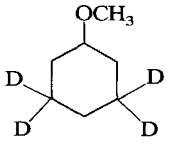
1



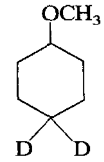
1a



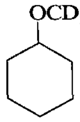
1b



1c



1d



1e

The FIK curves for the various labelled propyl eliminations from the molecular ions of **1b**, **1c** and **1d**, expressed as percentages of their sum, are presented in Figs 2–4. The points in the figures at $t = 10^{-6.5}$ s correspond with the percentages of the various labelled propyl eliminations occurring in the first field free region of the mass spectrometer. These eliminations could not be detected in the second field free region.

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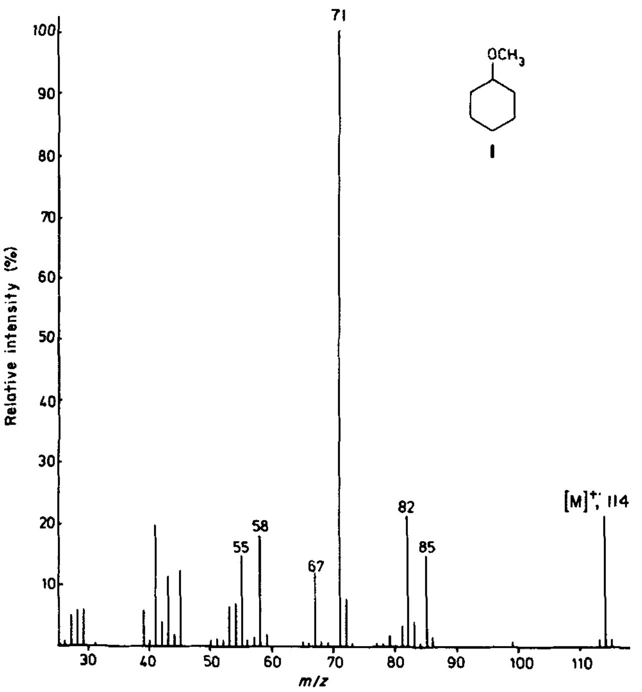


Figure 1. 70 eV mass spectrum of methoxycyclohexane.

The FIK curves for compounds **1a** and **1e** have not been shown as their molecular ions only lose an unlabelled propyl radical.

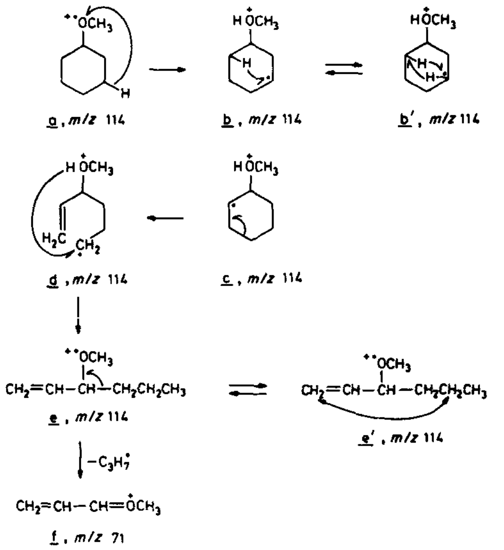
Propyl loss at $t \leq 10^{-10}$ s

Figures 2–4 show that at $t \leq 10^{-10}$ s the peak at *m/z* 71 generated from **1** shifts almost completely to *m/z* 72 for **1b** and to *m/z* 73 for **1c**, whereas it remains *m/z* 71 for **1d**. These results are in agreement with Scheme 1 which corresponds to the 'classical' elimination of propyl.[1]

Propyl loss at 10^{-10} s $\leq t \leq 10^{-9.3}$ s

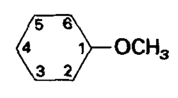
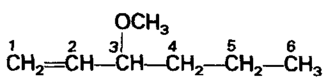
At 10^{-10} s a new process is beginning where, for compound **1b**, propyl is eliminated which contains all four deuterium atoms, as can be seen from the increase of the relative abundance of *m/z* 71 in Fig. 2. For compound **1c** this new process corresponds to the loss of propyl which contains only one deuterium atom to give *m/z* 74 (see Fig. 3), whereas no change is observed for the propyl loss from compound **1d** (see Fig. 4).

These observations can be explained if it is assumed that the longer lived ions of methoxycyclohexane have rearranged to those of 3-methoxyhexene-1 prior to the loss of propyl in the way shown in Scheme 3. The first step in this mechanism is the migration of a hydrogen atom from the 3-(or 5-)position to the methoxy group to give ion *b*.[5] Then an exchange takes place between one hydrogen atom at the 3-(or 5-)position and two hydrogen atoms at the 6-(or 2-)position. The next step is ring opening between C(4) and C(5) (or C(3)), followed by a shift of the



Scheme 3. Unorthodox propyl loss from the molecular ions of methoxycyclohexane with lifetimes of 10^{-10} s–$10^{-6.5}$ s. The hydrogen atom exchange process *b* ⇄ *b′* begins at 10^{-10} s, whereas the hydrogen atom exchange process *e* ⇄ *e′* is observed at $10^{-6.5}$ s.

Table 1. Partial mass spectra[a,b,c] of methoxycyclohexane and 3-methoxyhexene-1 and their D- and ^{13}C-labelled analogues at 70 eV (15 eV)

Compound	Labelled position	*m/z* 71	72	73	74	75
	d_0(**1**)	97.7(98.6)	2.2(1.4)	0.1(—)	—	—
	1-d_1(**1a**)	5.8(4.4)	90.5(93.2)	3.7(2.4)	—	—
	2,2,6,6-d_4(**1b**)	16.2[d](19.2)	77.4(76.0)	5.5(4.0)	0.9(0.8)	—
	3,3,5,5-d_4(**1c**)	10.9[d](6.9)	4.8(3.1)	66.1(68.7)	17.3(20.4)	0.9(0.8)
	4,4-d_2(**1d**)	89.2(93.9)	9.5(4.9)	1.3(1.2)	—	—
	—OCD_3(**1e**)	0.6(0.4)	—	1.9(1.2)	93.3(96.8)	4.2(1.6)
	2,2,5,5-d_4(**1f**)	3.5[d](3.4)	45.7(45.8)	48.7(47.9)	2.1(2.8)	—
	2-^{13}C(**1g**)	48.1(48.3)	51.1(51.0)	0.9(0.7)	—	—
 $\overset{1}{C}H_2{=}\overset{2}{C}H{-}\overset{3}{\underset{}{C}}H(OCH_3){-}\overset{4}{C}H_2{-}\overset{5}{C}H_2{-}\overset{6}{C}H_3$	d_0(**2**)	99.0(100)	1.0(—)	—	—	—
	5,5-d_2(**2a**)	97.1(98.8)	2.9(1.2)	—	—	—

[a] $\Sigma_{(71-75)} = 100.0$.

[b] Corrected for natural isotopic contributions.

[c] Average of at least three runs.

[d] In the unlabelled compound a peak is found at *m/z* 67, due to the loss of a methyl radical from the $[M-CH_3OH]^{+\cdot}$ ion. In the d_4-labelled analogues this peak could have been shifted to *m/z* 71 (complete label retention). High resolution measurements of *m/z* 71 showed this peak to be only C_4H_7O.

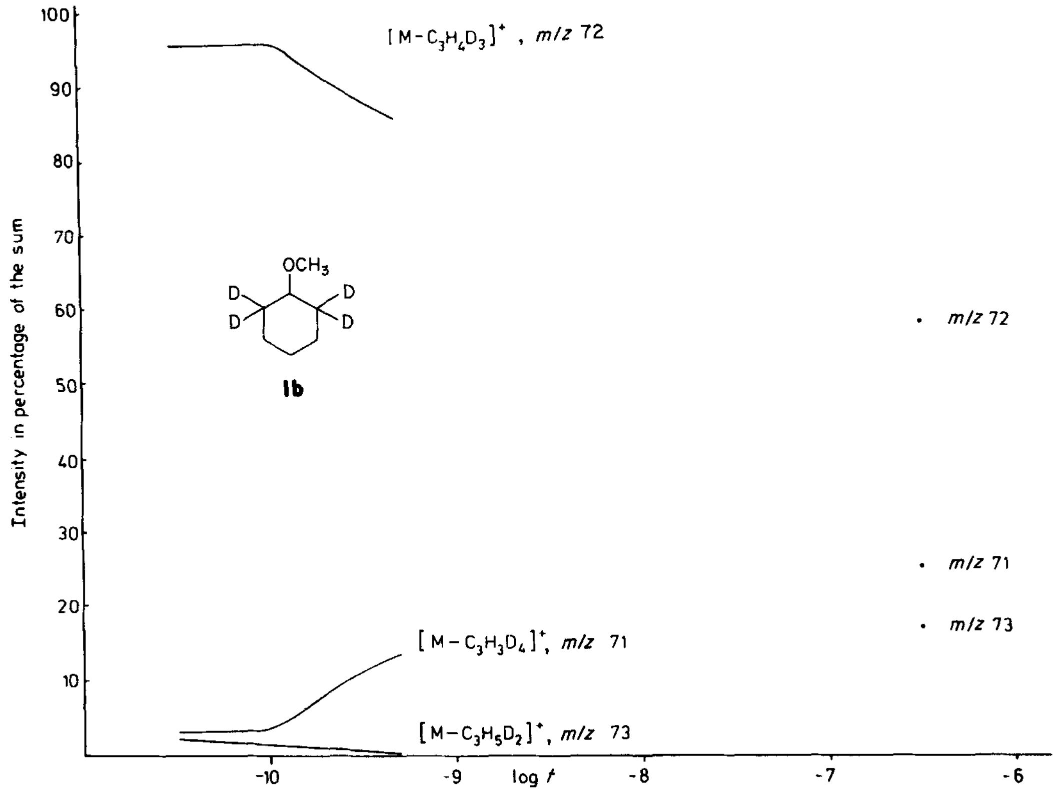


Figure 2. Loss of various labelled propyl radicals from ionized **1b** as a function of the molecular ion lifetime.

hydrogen atom from the oxygen atom to the radical position at C(4). The 3-methoxyhexene-1 ion generated in this way eventually eliminates a propyl radical by a simple cleavage reaction (see route $a \rightarrow b$ ($\rightleftarrows b'$) $\rightarrow c \rightarrow d \rightarrow e \rightarrow f$ in Scheme 3.)

Complete exchange between one hydrogen atom of the 3-(or 5-) position and two hydrogen atoms of the 6-(or 2-)position in ion b' would result in the elimination of 66.7% of a propyl radical having the 'classical' composition (and therefore indistinguishable from the

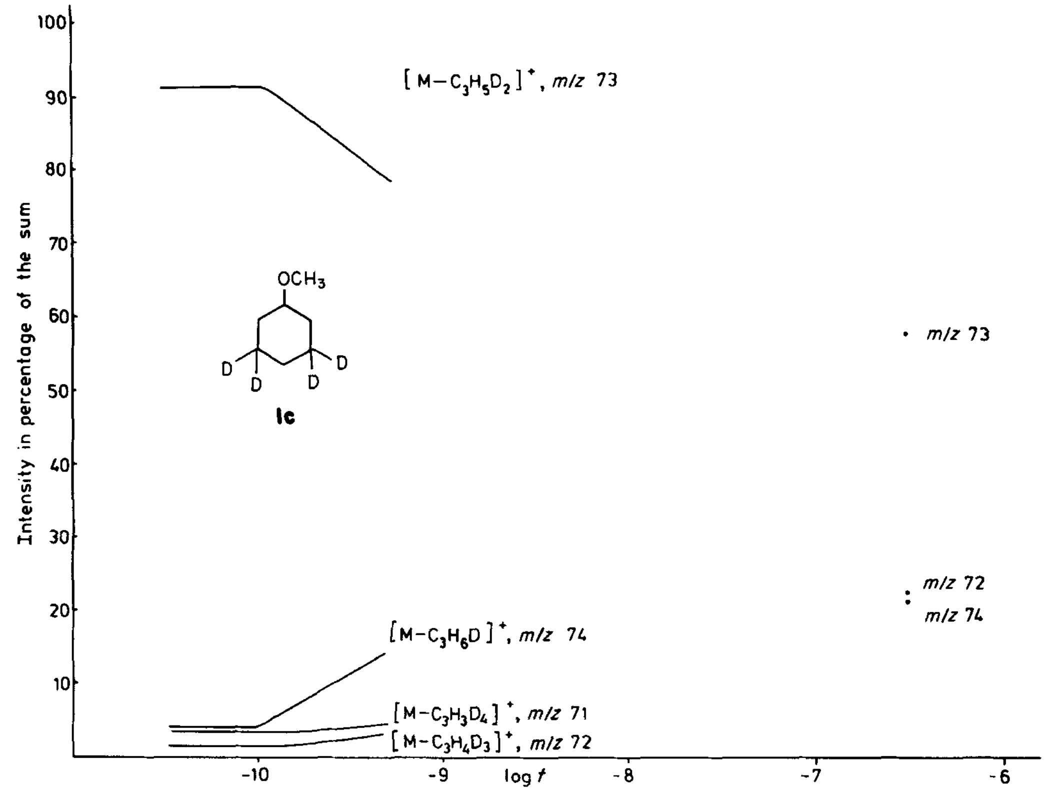


Figure 3. Loss of various labelled propyl radicals from ionized **1c** as a function of the molecular ion lifetime.

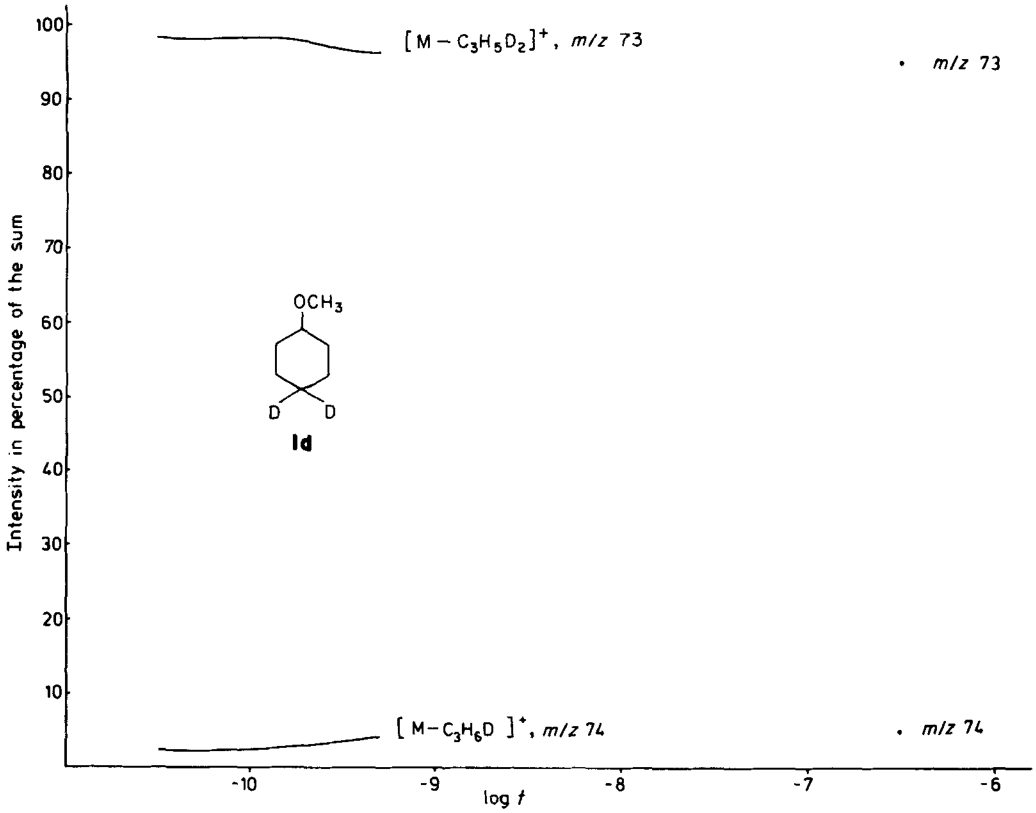
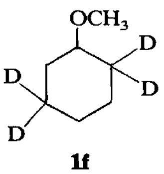


Figure 4. Loss of various labelled propyl radicals from ionized **1d** as a function of the molecular ion lifetime.

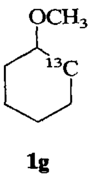
mechanism given in Scheme 1), that is three hydrogen atoms from the 2- and 6-position, two hydrogen atoms from the 4-position and two hydrogen atoms from the 3-(or 5-)position (composition A). The other 33.3% of the eliminated propyl radical, however, would then contain all four hydrogen atoms from the 2- and 6-position, but only one of the corresponding carbon atoms, both hydrogen atoms from the 4-position and only one hydrogen atom from the 3-(or 5-)position (composition B).

Within this picture it can be concluded from Figs 2 and 3 that at $10^{-9.3}$ s about half of the ions *c* have undergone such an exchange (via $b \rightleftarrows b'$) prior to the unorthodox loss of propyl. The 'classical' elimination of propyl (Scheme 1) most probably still plays a significant role at molecular ion lifetimes up to $10^{-9.3}$ s.

Further support for the mechanism presented in Scheme 3 has been obtained from the spectra of two other labelled analogues: 2,2,5,5-d_4-1-methoxycyclohexane (**1f**) and 2-^{13}C-1-methoxycyclohexane (**1g**). Exchange between deuterium atoms of the 2- and 5-position or between hydrogen atoms of the 3- and 6-position in the molecular ion of **1f** will not be effective in the expected eliminations of only $C_3H_5D_2^{\cdot}$ and $C_3H_4D_3^{\cdot}$ radicals. This is indeed the case as can be seen from Fig. 5 which shows that these radicals are eliminated from the molecular ion of **1f** in a constant ratio up to $10^{-9.3}$ s. The slightly higher percentage of the loss of $C_3H_5D_2^{\cdot}$ is most probably due to an isotope effect in step $a \rightarrow b$ (see Scheme 3). Finally, the molecular ion of compound **1g** eliminates up to $10^{-9.3}$ s equal amounts of unlabelled and ^{13}C-labelled propyl, which proves that C(2) and C(6) are not retained simultaneously in this radical. This observation invalidates the previously proposed mechanism summarized in Scheme 2.



1f



1g

Propyl loss at $t = 10^{-6.5}$ s

The percentages of the various labelled propyl radicals eliminated from the molecular ions of **1a**–**1f** in the first field free region are listed in Table 2. The results obtained for **1b** and **1c** show that 57–58% of the eliminated propyl has composition A and 21–25% composition B (see the preceding section for the meaning of A and B). 17–22% of the propyl radicals have a composition not found for shorter lived ions: two hydrogen atoms from the 2- and/or 6-position, three hydrogen atoms from the 3- and 5-positions, both hydrogen atoms of the 4-position and one carbon atom of the 2-(or 6-)position (composition C). These observations can be explained if in the 3-methoxyhexene-1 ion (ion *e′* in Scheme 3) an exchange is assumed to occur between the hydrogen atoms of the 1- and 5-position prior to elimination of the propyl radical (route $a \rightarrow b\ (\rightleftarrows b') \rightarrow c \rightarrow d \rightarrow e\ (\rightleftarrows e') \rightarrow f$ in Scheme 3).

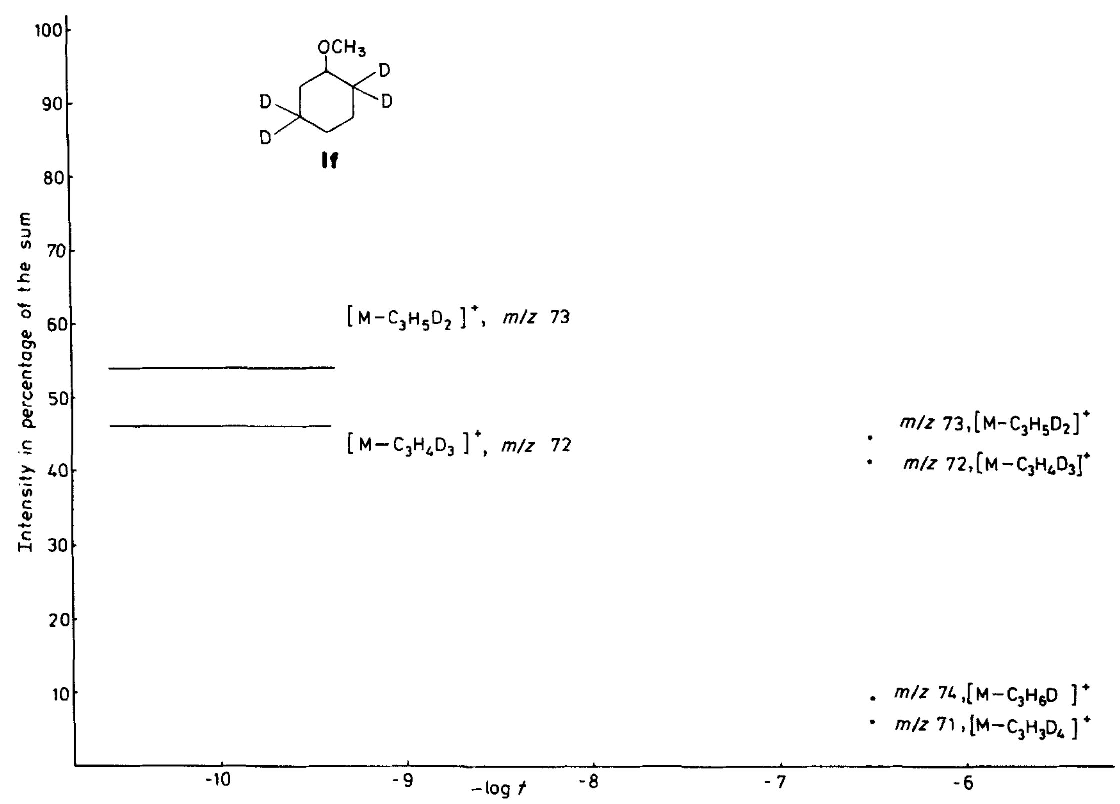
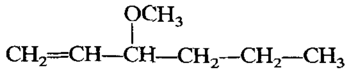


Figure 5. Loss of various labelled propyl radicals from ionized **1f** as a function of the molecular ion lifetime.

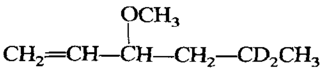
In Table 3 the observed and calculated percentages of the eliminations of various labelled propyl radicals are given at different lifetimes of the molecular ions. From this table it is clear that at $10^{-9.3}$ s about 50% of the ions have already undergone the exchange $b \rightleftharpoons b'$ (Scheme 3). In molecular ions with lifetimes as long as $10^{-6.5}$ s this exchange has been assumed to be complete, but not the exchange $e \rightleftharpoons e'$ (Scheme 3). From the observed percentage of elimination of propyl with composition C it can be calculated that the exchange $e \rightleftharpoons e'$ has occurred for 44–57%.

Support for the proposed exchange $e \rightleftharpoons e'$ in Scheme 3 has been obtained from the mass spectra of



$$CH_2{=}CH{-}\overset{\displaystyle OCH_3}{\overset{|}{C}H}{-}CH_2{-}CH_2{-}CH_3$$

2

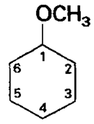
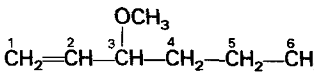


$$CH_2{=}CH{-}\overset{\displaystyle OCH_3}{\overset{|}{C}H}{-}CH_2{-}CD_2CH_3$$

2a

3-methoxyhexene-1(**2**) and its 5,5-d_2-analogue (**2a**). The EI spectrum of **2** (Fig. 6) is very similar to that of methoxycyclohexane (Fig. 1). The main differences between these spectra are the abundances of the

Table 2. Relative peak areas of metastable peaks in the first field free region at 70 eV, referring to the loss of a propyl radical from the molecular ions of methoxycyclohexane and 3-methoxyhexene-1 and their D- and ^{13}C-labelled analogues[a,b,c]

Compound	Labelled position	Loss of $C_3H_7^\cdot$	$C_3H_6D^\cdot$	$C_3H_5D_2^\cdot$	$C_3H_4D_3^\cdot$	$C_3H_3D_4^\cdot$	$^{13}CCH_2H_7^\cdot$
	d_0(**1**)	100	—	—	—	—	—
	1-d_1(**1a**)	>95	<5	—	—	—	—
	2,2,6,6-d_4(**1b**)	—	—	17	58	25	—
	3,3,5,5-d_4(**1c**)	—	21	57	22	—	—
	4,4-d_2(**1d**)	—	5	95	—	—	—
	—OCD_3(**1e**)	100	—	—	—	—	—
	2,2,5,5-d_4(**1f**)	—	9	44	41	6	—
	2-^{13}C(**1g**)	50	—	—	—	—	50
	d_0(**2**)	100	—	—	—	—	—
	5,5-d_2(**2a**)	16	51	33	—	—	—

[a] $\Sigma(C_3H_7 + C_3H_6D + C_3H_5D_2 + C_3H_4D_3 + C_3H_3D_4 + {}^{13}CC_2H_7) = 100.0$.
[b] Corrected for natural isotopic contributions.
[c] Average of at least three runs.

Table 3. Composition of propyl radicals eliminated from the molecular ions of methoxycyclohexane at $10^{-9.3}$ s and $10^{-6.5}$ s

Types of hydrogen atoms in the eliminated propyl		Percentages of observed and calculated compositions of the eliminated propyl						
		At $10^{-9.3}$ s			At $10^{-6.5}$ s			
			Calculated			Calculated		
		Observed	Complete exchange $b \rightleftarrows b'$ [a]	50% exchange $b \rightleftarrows b'$ [a]	Observed	Complete exchange $b \rightleftarrows b'$ [a]	Complete exchange $b \rightleftarrows b'$ and $e \rightleftarrows e'$ [a]	Complete exchange $b \rightleftarrows b'$ and 50% exchange $e \rightleftarrows e'$ [a]
3 H from 2- and 6-position 2 H from 5- and/or 3-position 2 H from 4-position	Composition A	83–86	66.7	83.3	57–58	66.7	55.5	61.2
4 H from 2- and 6-position 1 H from 5- or 3-position 2 H from 4-position	Composition B	13–14	33.3	16.7	21–25	33.3	5.6	19.4
2 H from 2- and/or 6-position 3 H from 3- and 5-position 2 H from 4-position	Composition C	0–3	—	—	17–22	—	38.9	19.4

[a] See Scheme 3.

molecular ions and the presence of a peak at *m/z* 58 in Fig. 1 which is due to the loss of two molecules of ethene from the molecular ion via a cycloreversion process. Such a process is not possible for the molecular ion of the non-cyclic compound **2**, which explains the almost complete absence of a peak at *m/z* 58 in its spectrum. The molecular ion of **2a** eliminates almost exclusively $C_3H_5D_2^{\cdot}$ in the ion source (see Table 1). However, Table 2 shows that in the first field free region 33% $C_3H_5D_2^{\cdot}$, 51% $C_3H_6D^{\cdot}$ and 16% $C_3H_7^{\cdot}$ are eliminated. An exchange between the deuterium atoms of the 5-position and at least two hydrogen atoms from the other end of the molecule, probably the 1-position, can explain these observations very well. Such an exchange, however, is not complete for the present case at $10^{-6.5}$ s as this would result in the elimination of 16.7% $C_3H_5D_2^{\cdot}$, 66.7% $C_3H_6D^{\cdot}$ and 16.7% $C_3H_7^{\cdot}$.

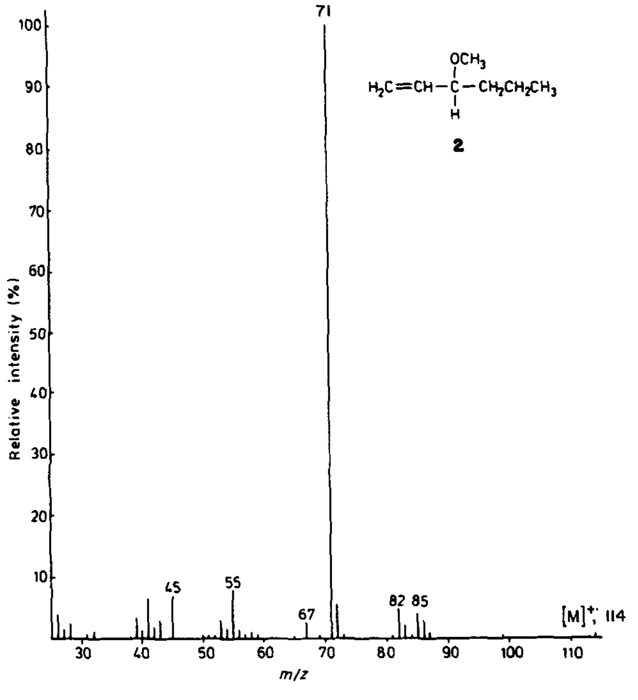


Figure 6. 70 eV mass spectrum of 3-methoxyhexene-1.

EXPERIMENTAL

Most electron impact mass spectra were obtained using an AEI MS-902 mass spectrometer operating at 70 eV and 15 eV and a source temperature of 150 °C. Samples were introduced through an all-glass heated inlet system at 150 °C.

Fragmentation reactions occurring in the first field free region of the MS-902 instrument were recorded by scanning the accelerating voltage at a constant electric sector potential. Some of these were also measured in a similar way on an AEI MS-50 instrument. The FIK measurements were performed using a Varian MAT 711 mass spectrometer as described before.[6]

Preparation of compounds

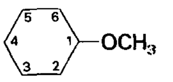
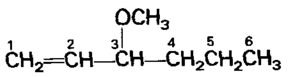
Unlabelled *methoxycyclohexane, trideuteromethoxycyclohexane,* 1-*deutero*-1-*methoxycyclohexane,* 2,2,6,6-*tetradeutero*-1-*methoxycyclohexane,* 3,3,5,5-*tetradeutero*-1-*methoxycyclohexane* and 4,4-*dideutero*-1-*methoxycyclohexane* were prepared as described by Klein and Smith.[2]

2,2,5,5-Tetradeutero-1-methoxycyclohexane. 2,2,5,5-Tetradeuterocyclopentanone, obtained by overnight exchange of cyclopentanone with D_2O/K_2CO_3 at 95 °C, was treated with potassium cyanide and formic acid to yield 2,2,5,5-tetradeutero-1-cyano-cyclopentanol-1.[7] This compound was reduced with $LiAlH_4$ to 2,2,5,5-tetradeutero-1-aminomethylcyclopentanol-1 and treated with $NaNO_2$ by known methods[7] to yield 2,2,5,5-tetradeuterocyclohexanone, which was converted into 2,2,5,5-tetradeutero-1-methoxycyclohexane as described by Klein and Smith.[2]

2-^{13}C-1-Methoxycyclohexane. For the synthesis of 2-^{13}C-1-methoxycyclohexane the same method was used as described above, starting with unlabelled cyclopentanone and using $K^{13}CN$ in the first reaction step.

5,5-Dideutero-3-methoxyhexene-1. Propionic acid was successively deuterated in the 2-position as described

Table 4. Measurements[a] of label content (%) of the labelled methoxycyclohexanes and 3-methoxyhexene-1 at 12 eV

Compound	Labelled position	Percentage d_0	d_1	d_2	d_3	d_4	^{13}C
	1-d_1(**1a**)	1.0	99.0	—	—	—	—
	2,2,6,6-d_4(**1b**)	—	1.0	2.2	3.1	93.7	—
	3,3,5,5-d_4(**1c**)	3.4	—	—	3.5	93.1	—
	4,4-d_2(**1d**)	0.7	15.6	83.7	—	—	—
	—OCD$_3$(**1e**)	—	—	2.0	98.0	—	—
	2,2,5,5-d_4(**1f**)	—	—	—	10.5	89.5	—
	2-^{13}C(**1g**)	10.6	—	—	—	—	89.4
 $\overset{1}{C}H_2=\overset{2}{C}H-\overset{3}{C}H(OCH_3)-\overset{4}{C}H_2\overset{5}{C}H_2\overset{6}{C}H_3$	5,5-d_2(**2a**)	2.7	17.8	79.5	—	—	—

[a] Average of at least five runs.

in the literature,[8] reduced by LiAlH$_4$ and treated with PBr$_3$ to yield 2,2-dideutero-1-bromopropane. This compound was coupled in a Grignard reaction with acrolein to yield 5,5-dideuterohexene-1-ol-3[9] which was converted into the corresponding methyl ether as described by Klein and Smith.[2]

Purification of compounds and label contents

All compounds used for the mass spectrometric measurements were purified by GC using a 15% carbowax 2000 column and/or a OV 17 silicone column. Positions and percentages of D and ^{13}C labelling were checked by NMR and determined by mass spectrometry, respectively (Table 4).

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REFERENCES

1. H. Budzikiewicz, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, p. 307, Holden Day, San Francisco (1967).
2. G. W. Klein and V. F. Smith, *J. Org. Chem.* **35**, 52 (1970).
3. (a) H.-D. Beckey, *Field Ionization Mass Spectrometry*, Pergamon, Oxford (1971); (b) P. J. Derrick, in *International Review of Science*, ed. by A. Maccoll, Vol. 5, Butterworths, London (1975); (c) N. M. M. Nibbering, *Int. J. Mass Spectrom. Ion Phys.* **45**, 343 (1982).
4. See D. J. Burinsky, G. L. Glish, R. G. Cooks, J. J. Zwinselman and N. M. M. Nibbering, *J. Am. Chem. Soc.* **103**, 465 (1981), and references cited therein.
5. Elimination of methanol from this ion is also possible. Klein and Smith (Ref. 2) have shown already that in the ion source 66% of the methanol loss occurs via a 1,3-elimination.
6. (a) P. Wolkoff, J. van der Greef and N. M. M. Nibbering, *J. Am. Chem. Soc.* **100**, 541 (1978); (b) J. van der Greef, F. A. Pinkse, C. W. F. Kort and N. M. M. Nibbering, *Int. J. Mass Spectrom. Ion Phys.* **25**, 315 (1977).
7. F. Geiss and G. Blech, *J. Labelled Compd.* **4**, 1119 (1968).
8. D. J. McAdoo and D. N. Witiak, *Org. Mass Spectrom.* **9**, 499 (1978).
9. A. I. Vogel, *Textbook of Practical Organic Chemistry*, 3rd edn, p. 255, Longman Green, London (1959).

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